REMARKS

Basis for the amendments

New claims 108 and 109 are presented. The recitation of "an expression vector (plasmid) or separate expression vectors (plasmids)" is supported, *e.g.*, by the paragraph at page 24, lines 15-26, the paragraph from page 19, line 22 to page 20, line 5; and page 40, line 14.

Nonelected claim 100 is amended to depend in the alternative from new product claims 108 and 109.

The amendments add no new matter to the disclosure.

Inventorship

Concurrently with the reply filed on 13 December 2006, applicant filed a request to correct the inventorship in this application under 37 C.F.R. § 1.48(b). The request is not acknowledged in the final Office action, and to date, the Office has not otherwise taken action on the request. Applicant requests that the examiner take appropriate action with respect to this matter.

Objection to the abstract

The Office has objected to the amended abstract as introducing new matter in violation of the prohibition of 35 U.S.C. § 132. Applicant maintains that the amended abstract is fully supported by the application as filed and accordingly traverses the objection.

The reasons that the amended abstract finds support in the disclosure as filed are the same reasons that similar language in the claims has proper basis. These reasons are discussed at length in connection with applicant's traversal of the rejections under the written description requirement of § 112, below, which are incorporated into this traversal of the objection. For those reasons, applicant requests that the examiner reconsider and withdraw the objection.

Rejection under 35 U.S.C. § 112, first paragraph

Claims 70-75, 98, 99, 103, and 104 have been rejected under the written description requirement of § 112, first paragraph. Applicant respectfully traverses the rejection.

Applicant respectfully submits that the Office's analysis does not take into account all of the evidence in the disclosure as filed and is therefore not properly based. To address the Office's concern that applicant's position is based on attorney argument rather than evidence, applicant additionally submits with this reply a declaration under 37 C.F.R. § 1.132 by one of the inventors, Mitchell E. Reff. Applicant requests that the Office reconsider and withdraw the written description rejections in view of this evidence and the remarks set forth below.

Secretory sequences

The Office states that the claims encompass cells that express the recited nucleic acid sequences but lack regulatory nucleic acid sequences for secreting the antibody product. The Office believes that such cells are not described in the specification, and thus that claims 70, 72, and the claims that depend from them lack proper basis in the original disclosure.

As a threshold issue, applicant notes that none of the claims *requires* expression without secretion, and none state that sequences for secretion are absent from the claimed host cell. The Office's focus on embodiments that are merely encompassed by the claims is improper. The written description requirement is satisfied as to a generic claim where the specification describes the invention *as claimed*, not any particular species that the claim may encompass. *See Utter v. Hiraga*, 845 F.2d 993, 998, 6 USPQ2d 1709, 1714 (Fed. Cir. 1998); *see also* MPEP § 2163.

As Dr. Reff explains in his declaration, the specification as filed does contain a description of the generic invention of claim 70. He states that the recited nucleic acid sequences are described. Reff. dec. ¶ 5. He explains that host cells for various purposes are described throughout the specification, and that the uses for such cells were well known in the art. Reff dec. ¶¶ 10-11. Information which is well known in the art need not be described in detail in the specification. *See, e.g., Hybritech, Inc. v. Monoclonal Antibodies, Inc.*, 802 F.2d 1367, 1379-80, 231 USPQ 81, 90 (Fed. Cir. 1986). "If a skilled artisan would have understood the inventor to be

in possession of the claimed invention at the time of filing, even if every nuance of the claims is not explicitly described in the specification, then the adequate description requirement is met." MPEP § 2163 (Written Description Guidelines). Dr. Reff states his opinion that "the specification would have informed a person skilled in this art that our invention included a host cell having the characteristics" recited in claim 70. Reff dec. ¶ 5.

The Office's position appears to be based in part on the assumption that a "host cell" is limited to cells that are used for expressing exogenous nucleic acid sequences and for secreting their expression products. Dr. Reff explains that the scope of host cells described in the specification is broader. At ¶ 6 of his declaration, he states his belief

> that a person skilled in the field of the invention reading the application in November 1992 would have understood the term "host cell" to refer to a cell into which exogenous nucleic acid had been introduced or, depending on the context, to a cell that would be suitable for such introduction.

With reference to the specification, Dr. Reff notes that the application describes several different kinds of host cells used for different purposes. He observes that while some host cells described in the application are used for protein expression, other host cells and uses for host cells are also described. Reff dec. ¶ 7. He notes, for example, that the specification describes cells for expanding nucleic acid sequences, such as those described at page 21, lines 22-24 (preparation of cDNA "from RNA which was in turn derived from cells transfected with a human IgG1 vector"). Reff dec. ¶ 10. Dr. Reff explains, *id.*:

> As persons skilled in the art understood, such host cells did not need to be capable of expressing an exogenous nucleic acid to be useful; such cells could be used for expanding the nucleic acid. The use of such host cells for such purposes was broadly known to molecular biologists in November 1992.

It is clear that the host cells described in the specification are not limited to host cells for expression. Instead, host cells useful for any of the purposes described in the specification, such as for expanding nucleic acid sequences, form a part of the invention. For example, as Dr. Reff notes at ¶ 11 of his declaration, U.S. Patent No. 5,648,267, which by express incorporation forms a part of the original disclosure in this application, describes *E. coli* host cells that are used to expand a cloned nucleic acid.

Dr. Reff specifically addresses the question of whether the application describes host cells comprising immunoglobulin heavy chain and light chain nucleic acid sequences, but that do not necessarily secrete antibody proteins. He concludes that "the application would have informed a person of ordinary skill that the capability to secrete antibody proteins was not an essential or necessary feature of host cells such as those having the characteristics" recited in claim 70. Reff dec. ¶ 12. He notes in particular that at page 19, lines 22-29, the application describes a process of assembling separately expressed immunoglobulin chains *in vitro* to produce an antibody. He states that a "person skilled in this field in November 1992 would have recognized that such a technique would not depend on the use of cells that secreted the immunoglobulin chains." *Id.*

Finally, Dr. Reff reiterates his opinion that the application describes the generic invention of a host cell having the features recited in claim 70:

> [T]he application describes … host cells that are used to produce antibody proteins, and those that are not; as well as host cells that are capable of secreting antibody proteins, and those that need not secrete antibody proteins. I believe the application would have conveyed to a person skilled in molecular biology in November 1992 that all such host cells are useful in methods that were well known in the art for expanding or expressing nucleic acid sequences encoding immunologically active anti-CD20 antibodies according to the procedures described in the patent application.

Reff dec. ¶ 17.

In view of the declaration evidence demonstrating that a person skilled in the art in November 1992 would have understood the specification to provide a description of the generic invention of claim 70, without reference to a requirement for expression or secretion, applicant requests that the examiner reconsider this aspect of the rejection.

Plasmids

The Office takes the position that because the exemplified expression vector is a plasmid expression vector, the written description only supports claims to host cells that contain plasmid expression vectors. This rejection is advanced against all of the claims.

The Office's position is incorrect for at least two reasons. First, as explained above, the description of host cells is not limited to cells that are required to be capable of expressing or secreting the specified nucleotide sequences. Thus, the invention relates generally to host cells comprising the specified nucleic acid sequences, not only to those that contain plasmids or plasmid expression vectors. Second, a variety of vectors suitable for use in the invention, and not only plasmid expression vectors, are expressly identified in the specification.

Dr. Reff identifies one portion of the specification that explicitly describes a variety of methods that are suitable for incorporating nucleic acids into host cells. He notes that at page 24, lines 20-25, it "describes methods that 'include, but are not limited to, transfection (including electrophoresis and electroporation), cell fusion with enveloped DNA, microinjection, and infection with intact virus.'" Reff dec. ¶ 8. Indeed, Dr. Reff states that one could have microinjected host cells with just the nucleic acid of interest. *Id.* The methods identified in the specification are illustrated in greater detail in the book chapter by A.A.G. Ridgway that is cited at the same passage of the specification, and that Dr. Reff discusses in his declaration (copy appended to the declaration as an exhibit). This chapter teaches that "[t]he term *vector* in molecular biology has a broad definition." *See* Reff dec. ¶ 9. With reliance on the evidence at pages 470-472 of the Ridgway chapter, Dr. Reff concludes that

> as a person skilled in molecular biology would have immediately appreciated from the reference to the various techniques we identified in our application, the methods useful for introducing nucleic acids into host cells were not limited to transfection with a plasmid.

Id.

The Office appears to reason that because the claims in some cases recite particular functions, such as the capability to express and secrete a protein, but do not affirmatively recite that they contain a transfected plasmid, the claims are deficient. In particular, it states that "[t]he claims encompass host cells that only contain the specific nucleic acid recited in the claims wherein such host cells are not disclosed in the specification as originally filed."

Dr. Reff addresses this reasoning. He states that "[o]ne skilled in this field in November 1992 would have understood that the components and attributes of various host cells are determined according to the particular functions that such host cells need to perform." Reff dec.

¶ 16. Moreover, "[a] person skilled in the field would have understood that the presence of the necessary components and attributes for achieving a stated purpose is implicit in a reference to a particular cell as a 'host cell' for that purpose. *Id.* Thus, one skilled in the art would not have understood the claims to require cells that "only contain the specific nucleic acid recited in the claims." Instead, as Dr. Reff explains, the disclosure conveys – and the claims implicitly require – the molecular components necessary for the various uses of host cells.

As evidence supporting this understanding of the meaning and implications of the term "host cell" in the art, applicant notes that the Office, as a matter of longstanding practice, has granted claims to "host cells" without reference to functional attributes or molecular components present in the host cells other than identified exogenous DNA of interest. Such patents include, for example:

U.S. Patent No. 5,235,049 Priority to January 1990 Art Unit 1813

Nucleic Acid Sequences Encoding a Soluble Molecule (SICAM-1) Related to But Distinct from ICAM-1

2. A purified and isolated nucleotide sequence encoding naturally-occurring human soluble intercellular adhesion molecule-1, said naturally-occurring human soluble intercellular adhesion molecule-1 having the amino acid sequence set forth in Fig. 1.

4. A host cell containing the DNA sequence of claim 2.

U.S. Patent No. 5,436,155 Priority to December 1991 Art Unit 1812

Isolated DNA Encoding a Somatostatin Receptor

18. An isolated DNA segment having a sequence encoding a somatostatin receptor polypeptide wherein the segment is hybridizable to a DNA segment having a nucleotide sequence selected from the group consisting of Sequence ID numbers 1, 3, 5, 7, 9 and 11 under standard hybridization conditions.

20. A recombinant host cell which incorporates an isolated DNA segment in accordance with claim 18 or 19.

U.S. Patent No. 5,622,838 Priority to July 1984 Art Unit 1805

DNA Preparation Coding For Ricin A and Methods of Using Same

1. A biologically pure sample of a DNA molecule, said DNA molecule comprising at least a substantial portion of: (a) nucleotides 1-801 of the nucleotide sequence shown in Table 1, or (b) a nucleotide sequence that is equivalent by virtue of degeneracy of the genetic code to nucleotides 1-801 of the nucleotide sequence

shown in Table 1, wherein said portion encodes a polypeptide which inhibits protein synthesis at 60S subunits of ribosomes.

15. A host cell comprising the DNA molecule of claim 1.

U.S. Patent No. 6,066,498 Priority to March 1995 Art Unit 1644

Compositions for the Treatment and Diagnosis Of Immune Disorders

1. An isolated nucleic acid molecule comprising a nucleotide sequence selected from The group consisting of:

(a) the nucleotide sequence contained in SEQ ID NO:3, in a plasmid within E. coli clone 10-C as deposited with the NRRL (NRRL Accession No. B-21390) or in the cDNA insert contained within E. coli clone 10-X as deposited with the NRRL (NRRL Accession No. B-21455);

(b) the nucleotide sequence contained in SEQ ID NO:4 or in a plasmid within E. coli clone 57-E as deposited with the NRRL (NRRL, Accession No. B-21391);

(c) the nucleotide sequence contained in SEQ ID NO:5 or in a plasmid within E. coli clone 105-A as deposited with the NRRL (NRRL Accession No. B-21392);

(d) the nucleotide sequence contained in SEQ ID NO:6 or in a plasmid within E. coli clone 106-H as deposited with the NRRL (NRRL Accession No. B-21393); and

(e) the nucleotide sequence contained in SEQ ID NO:7 or in a plasmid within E. coli clone 161-G as deposited with the NRRL (NRRL Accession No. B-21394).

10. A genetically engineered host cell containing the nucleic acid of claim 1 or 8.

U.S. Patent No. 6,521,448 Priority to August 1997 Art Unit 1644

Porcine MHC Class I Genes and Uses Thereof

1. An isolated nucleic acid molecule comprising the nucleotide sequence of SEQ ID NO:1.

4. A cell line containing the isolated nucleic acid molecule of claim 1.

U.S. Patent No. 7,132,281 Priority to December 1998 Art Unit 1644

1. A mammalian host cell line comprising polynucleotides encoding the heavy and light chains of a human monoclonal antibody that competes for binding to human CTLA-4 with an antibody comprising the heavy chain FR1 through FR4 amino acid sequence in SEQ ID NO: 1 and the light chain FR1 through FR4 amino acid sequence in SEQ ID NO: 14, wherein said competing human monoclonal antibody inhibits binding of human CTLA-4 to human B7-1 and human B7-2 and wherein said competing human monoclonal antibody comprises a light chain that utilizes a human A27 Vκ gene.

The Office's assertion that the written description is limited to plasmid expression vectors is at odds with the evidence of the written description itself. Plainly, the disclosure describes host cells generally, as claimed. Reconsideration of this aspect of the rejection is requested.

Membrane-bound antibodies

The Office takes the view that "[t]he claims encompass host cells that express nucleic acids encoding membrane bound anti-CD20 antibody, yet there is no disclosure of such cells in the specification as originally filed." This aspect of the rejection is directed particularly to claims 70, 72, and the claims that depend from them.

What the original disclosure describes, and what the claims recite, is an immunologically active anti-CD20 antibody. The term "antibody" is not given a limiting definition in the specification. Thus, one skilled in the art would recognize that the term, as read in the context of the present specification, should be understood to have its conventional meaning as it is used in the art. Reff dec. ¶ 14.

As Dr. Reff states in his declaration, "'[a]ntibodies' are broadly described in the application." Reff dec. ¶ 14. Citing a portion of a 1991 immunology textbook, he explains that the "structural and functional characteristics of the different classes of antibodies were well known in the art by November 1992." *Id.* In particular, it was known that naturally occurring "antibodies" included both soluble and membrane-bound forms. Dr. Reff thus concludes that the meaning of "antibody" in the specification would be understood to cover both soluble and membrane-bound antibodies, in accord with the conventional usage of the term in the art. *See id.*

Applicant also notes that the Office has acknowledged that the antibody art "is a mature technology where the level of skill is high and advanced." U.S. Patent and Trademark Office, *Synopsis of Application of Written Description Guidelines*, March 2000, at 60. "What is conventional or well known to one of ordinary skill in the art need not be disclosed in detail." MPEP § 2163 (Written Description Guidelines).

In view of Dr. Reff's opinion, the evidence indicates that the specification as filed describes the genus of antibodies, including both soluble and membrane-bound antibodies, according to the conventional understanding of the generic term as recognized in the art. The

examiner's focus on a particular subgenus of antibodies that is not expressly required by the claims is improper. Compliance with the written description requirement must be assessed with respect to support for the invention as claimed, not support for any particular species or subgenus that the claims encompass. *See Utter*, *supra.*

Observations on new claims 108 and 109

Applicant notes that new claims 108 and 109 address all of the issues raised above. In particular, these claims depend from claim 98, which stands rejected only for the absence of an affirmative recitation of a plasmid. Claims 108 and 109 recite specifically that the host cell comprises expression vector(s) or expression plasmid(s). Accordingly, these claims should be found to be free of all stated grounds of rejection.

Conclusion

Applicant believes that this reply fully responds to the outstanding Office action.

Applicant requests that the Office withdraw the outstanding objection and rejection and indicate that all of the pending claims are allowable. Applicant reiterates the request that the restriction requirement between the elected product claims and the dependent method claims be withdrawn upon a finding that the product claims are allowable.

Respectfully submitted,

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